

PATENT/Docket No. PC10901A

Appl. No. 09/779,413

Filing Date: February 8, 2001

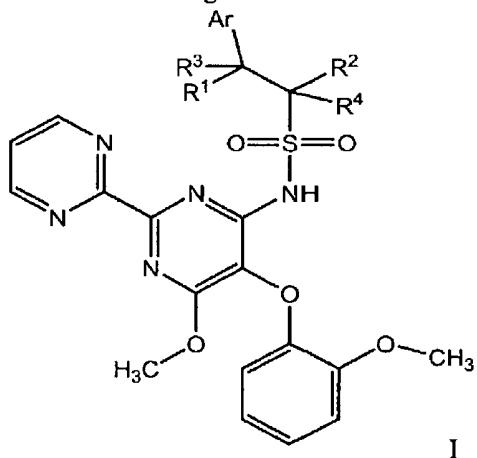
Amtd. dated July 14, 2004

Reply to Office action of February 17, 2004

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously presented) A method for the treatment or prophylaxis of an endothelin-mediated disorder in a companion animal which comprises administering an effective amount, wherein the free blood plasma concentration after twenty four hours remains above the concentration providing efficacy for said endothelin-mediated disorder, of a compound of formula I or a veterinarly acceptable salt thereof to the companion animal, compound of formula 1 having the formula:



wherein R<sup>1</sup> and R<sup>2</sup> each represent H, or together represent a second carbon-carbon bond between the carbon atoms to which they are attached;

when R<sup>1</sup> and R<sup>2</sup> each represent H, then R<sup>3</sup> and R<sup>4</sup> also represent H;

when R<sup>1</sup> and R<sup>2</sup> together represent a second carbon-carbon bond between the carbon atoms to which they are attached, then R<sup>3</sup> and R<sup>4</sup> independently represent H or C<sub>1</sub>-C<sub>6</sub> alkyl;

Ar represents:

phenyl or naphthyl, which groups are optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl (which may itself be substituted by one or more substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl) and N((C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>), halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub> OH and C<sub>1</sub>-C<sub>3</sub> alkylene dioxy, or

a 5- or 6-membered heteroaryl ring containing up to 4 heteroatoms selected from N, O and S, which group is optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), and N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>.

2. (Previously presented) A method according to claim 1, wherein the companion animal is a cat, a dog or a horse.

3. (Previously presented) A method according to claim 1 or 2, wherein the endothelin mediated disorder is hypertension, congestive heart failure or chronic renal failure.

FORM AMEND  
Rev. 5/27/03

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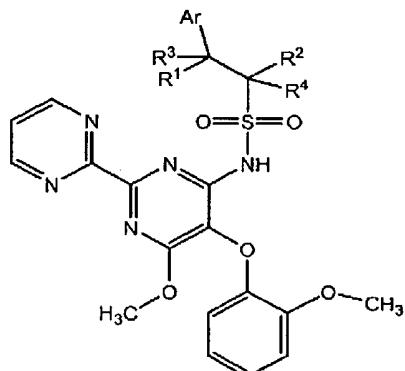
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4. (Previously presented) A method according to claim 1, wherein R<sup>1</sup> and R<sup>2</sup> each represent H.
5. (Previously presented) A method according to claim 1, wherein R<sup>3</sup> and R<sup>4</sup> each represent H.
6. (Currently amended) A method according to claim 1 wherein Ar represents phenyl or naphthyl, naphthyl, or thiaryl, which groups are optionally substituted by one or more groups selected from C<sub>1-6</sub> alkyl, halo, CF<sub>3</sub>, C<sub>1-6</sub> alkoxy, CO<sub>2</sub>H and C<sub>1-6</sub> alkoxy carbonyl.
7. (Previously presented) The method according to claim 1, wherein Ar is phenyl.
8. (Previously presented) The method of claim 1, wherein the endothelin mediated disorder is congestive heart failure.
9. (Previously presented) The method of claim 1, wherein the endothelin mediated disorder is chronic renal failure.
10. (Currently amended) A formulation containing a compound of formula I or a veterinarily acceptable salt thereof:



wherein R<sup>1</sup> and R<sup>2</sup> each represent H, or together represent a second carbon-carbon bond between the carbon atoms to which they are attached;

when R<sup>1</sup> and R<sup>2</sup> each represent H, then R<sup>3</sup> and R<sup>4</sup> also represent H;

when R<sup>1</sup> and R<sup>2</sup> together represent a second carbon-carbon bond between the carbon atoms to which they are attached, then R<sup>3</sup> and R<sup>4</sup> independently represent H or C<sub>1</sub>-C<sub>6</sub> alkyl;

Ar represents:

phenyl or naphthyl, which groups are optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl (which may itself be substituted by one or more substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, NH<sub>2</sub>, NH(C<sub>1-6</sub> alkyl) and N((C<sub>1-6</sub> alkyl)<sub>2</sub>), halo, C<sub>1-6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1-6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1-6</sub> alkyl), N((C<sub>1-6</sub> alkyl)<sub>2</sub> OH and C<sub>1-3</sub> alkylene dioxy, or

a 5- or 6-membered heteroaryl ring containing up to 4 heteroatoms selected from N, O and S, which group is optionally substituted by one or more groups selected from C<sub>1-6</sub> alkyl, halo, C<sub>1-6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1-6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1-6</sub> alkyl), and N((C<sub>1-6</sub> alkyl)<sub>2</sub>;

FORM AMEND  
Rev. 5/27/03

Page 3 of 6

**PATENT/Docket No. PC10901A**

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the formulation characterized in that it is suitable~~adapted~~ for administration to a companion animal, wherein the free blood plasma concentration of compound of formula 1 after twenty four hours remains above the concentration providing efficacy for said endothelin-mediated disorder.

11. (Currently amended) A formulation according to claim 10, which is suitable~~adapted~~ for oral administration ~~and has a taste attractive~~ to the companion animal.

12-14. (Canceled)

FORM AMEND  
Rev. 5/27/03

Page 4 of 6